Interim Guidance for the Management of Chronic Hepatitis C Infection

Federal Bureau of Prisons
Clinical Practice Guidelines

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1. Purpose and Overview

From the time Hepatitis C virus (HCV) was first identified as a major cause for chronic hepatitis, finding a treatment that was effective, easy to administer, and relatively free from side effects has been elusive. However, starting in 2011, four new medications that act directly against HCV have been approved for treatment of this condition, and more are expected in the future. The preferred treatment regimen has changed with each of the new recently approved, direct-acting antiviral medications (DAAs)—resulting in rapidly changing clinical guidelines and treatment recommendations. While an all-oral, interferon-free regimen is currently available for certain genotypes, even newer medications are expected to become available that will be safer, simpler, and more effective. In the midst of this rapidly changing treatment landscape, the most recently published guidance on HCV treatment (*www.hcvguidelines.org*) indicates that it is reasonable to postpone treatment for cases with less advanced fibrosis, pending the expected availability of better treatments in the very near future.

The purpose of this document is to provide interim guidance for the treatment of chronic HCV infection in the federal inmate population. During this time of transition, the BOP has established treatment priorities for inmates who have a more urgent need for intervention, as described below. The recommended treatment regimens, as well as medication dosing, monitoring, and special considerations, are also discussed. The appendices cover detailed medication information, monitoring recommendations, and management of hematologic changes.

2. Priorities for Treatment

The following clinical scenarios involving chronic HCV infection should be prioritized for treatment:

- Advanced hepatic fibrosis/cirrhosis
- Liver transplant recipients
- HIV co-infection
- Comorbid medical conditions associated with HCV, e.g. cryoglobulinemia and certain types of lymphomas
- Continuity of care for newly incarcerated BOP inmates who were being treated at the time of incarceration

The degree of fibrosis may be determined in several ways: The AST-to-platelet ratio index (APRI) correlates fairly well with more advanced fibrosis/cirrhosis, having a sensitivity of 76% and specificity of 72%. The formula for calculating the APRI score is [(AST/AST ULN) x 100 / (platelet count x 10^3/μL / 1,000)]. The BOP will prioritize for treatment inmates who have an APRI score ≥ 1.0, or whose APRI score is between 0.7 and 1.0 along with other findings suggestive of advanced fibrosis (low albumin or platelets, elevated bilirubin or INR). Although a liver biopsy is no longer required unless otherwise clinically indicated, results of a prior liver biopsy may be used to meet the advanced fibrosis criteria. Abdominal imaging studies such as ultrasound or CT scan also may identify findings consistent with cirrhosis.

In addition to the above, inmates being considered for treatment of HCV should have no contraindications to any component of the treatment regimen, should not be pregnant, should have sufficient time remaining on their sentence in the BOP to complete a course of treatment, and should demonstrate a willingness and an ability to adhere to a rigorous treatment regimen and to abstain from high-risk activities while incarcerated.

3. Recommended Treatment Regimens

Note: *Current guidelines do not recommend the use of boceprevir or telaprevir when initiating treatment for HCV. However, if treatment with boceprevir or telaprevir has already been initiated, it should be continued as long as treatment criteria are met.*

The recommended treatment regimen still depends on the genotype and prior HCV treatment history, as noted below. The AASLD-IDSA preferred treatment regimen is listed; alternative regimens may be considered on a case-by-case basis.

a. HCV-1 and treatment naïve or relapser following peginterferon/ribavirin (PEG/RBV) therapy:

- *Preferred regimen:* sofosbuvir + ribavirin + peginterferon for 12 weeks
- If peginterferon is contraindicated, consider sofosbuvir + simeprevir +/- ribavirin for 12 weeks.

b. HCV-1 and non-responder (partial or null responder) to prior HCV treatment with PEG/RBV:

- Sofosbuvir + simeprevir +/- ribavirin for 12 weeks, regardless of HCV-1 subtype (a or b).

c. HCV-1 and non-responder to prior HCV treatment with PEG/RBV/HCV protease inhibitor:

- Sofosbuvir + ribavirin + peginterferon for 12 weeks

d. HCV genotypes 2 through 6, treatment naïve, relapsers, or non-responder to prior treatment with PEG/RBV:

- **HCV-2** = sofosbuvir + ribavirin for 12 weeks (extended to 16 weeks for prior non-responders with cirrhosis)
- **HCV-3** = sofosbuvir + ribavirin for 24 weeks
- **HCV-4** = sofosbuvir + ribavirin + peginterferon for 12 weeks. If peginterferon is contraindicated, sofosbuvir + ribavirin for 24 weeks is recommended.
- **HCV-5** = sofosbuvir + ribavirin + peginterferon for 12 weeks*
- **HCV-6** = sofosbuvir + ribavirin + peginterferon for 12 weeks*

* *If peginterferon is contraindicated, there are no alternative regimens recommended for HCV genotype 5 or 6.*

e. Recommended medication doses for patients with compensated liver disease, normal renal function, and normal hematologic indices:

- Peginterferon alfa-2A – 180 micrograms subcut once weekly
- Peginterferon alfa-2B – consult *Appendix 1* for weight-based dosing.
- Ribavirin – According to the newest AASLD-IDSA guidance, the dose of ribavirin is based on a patient's weight for sofosbuvir- or simeprevir-based regimens. For patients ≥ 75 kg, the ribavirin dose is 600 mg by mouth twice daily. For those < 75 kg, the dose is 1000 mg/day divided in two doses, 400 mg and 600 mg. Note that the ribavirin dose recommended for sofosbuvir- or simeprevir-based regimens differs somewhat from the dose used for earlier regimens such as peginterferon + ribavirin +/– boceprevir or telaprevir. Ribavirin is recommended to be taken with food.
- Simeprevir – 150 mg by mouth once daily, with food
- Sofosbuvir – 400 mg by mouth once daily, with or without food

f. The following treatment regimens are no longer recommended for the above clinical scenarios unless completing a course of treatment that has already been started:

- Monotherapy with interferon, ribavirin, or any direct-acting antiviral agent
- Dual therapy with peginterferon and ribavirin
- Triple therapy with peginterferon, ribavirin, and either boceprevir or telaprevir

4. Monitoring

Updated guidelines have not been published on monitoring the newest medication regimens. However, the following general statements may be made:

- HCV-1a cases being considered for an alternative regimen using simeprevir in combination with peginterferon and ribavirin (without sofosbuvir) must first be tested for the NS3 Q80K polymorphism, found in BEMR as Hep C Genosure NS3/4 A Drug Resistance. Patients with the Q80K polymorphism are not candidates for this treatment regimen. A possible exception to this is an HCV-1a genotype that is being treated with a combination of simeprevir and sofosbuvir.
- Pregnancy testing is required prior to treatment with ribavirin-containing regimens, and then periodically during and after treatment.
- For all regimens, HCV viral loads need to be drawn prior to treatment and at the end of treatment, as well as either 12 or 24 weeks after treatment completion for those with undetectable end of treatment viral loads.
  - For sofosbuvir regimens, the only on-treatment viral load is drawn after 4 completed weeks of treatment, primarily to assess for adherence.
  - For simeprevir-containing regimens, viral loads need to be drawn after treatment weeks 4, 12, and 24 to assess response to treatment.
- Monitoring of interferon and/or ribavirin-containing regimens is the same as before and is included as *Appendix 5*.

5. Special Considerations

Chronic kidney disease:

- Simeprevir and sofosbuvir may be used with GFRs ≥ 30, but sofosbuvir is not recommended for GFRs < 30, and neither medication is recommended for use with hemodialysis.
- Ribavirin doses must be decreased with GFRs < 50. For GFRs 30–50, ribavirin is dosed 200 mg alternating every other day with 400 mg. For GFR < 30 including hemodialysis, the ribavirin dose is 200 mg daily.
- Pegylated interferon is dosed differently depending on which form is used. For a GFR < 30 or hemodialysis, peginterferon alfa-2A is dosed 135 micrograms/week, and peginterferon alfa-2B is dosed 1 microgram/kg/week. Regular interferon alfa dosed 3 million units three times/week is an alternative in ESRD/hemodialysis cases.

Decompensated cirrhosis or liver transplant recipients:

- Medication doses and regimens may differ from those in compensated liver disease. Such cases should be managed in consultation with an experienced clinician/specialist.
- Decompensated cirrhosis (e.g., Child-Turcotte-Pugh/CTP class B or C) is still a contraindication to interferon-containing regimens.

HIV co-infection:

- HCV medication regimens are the same for HIV co-infected patients as for HIV-negative patients.
- Antiretroviral medication changes may be necessary for patients with HIV co-infection being considered for HCV treatment, due to potential drug interactions between sofosbuvir or simeprevir and certain antiretrovirals.
  - Sofosbuvir should not be used with didanosine, zidovudine, or tipranavir.
  - Simeprevir may be used only with abacavir, tenofovir, emtricitabine, lamivudine, raltegravir, rilpivirine, maraviroc, and enfuvirtide.

Reference

AASLD, IDSA, IAS–USA. HCV testing and linkage to care. Recommendations for testing, managing, and treating hepatitis C. Available at: http://www.hcvguidelines.org/ Accessed May 2014.

Appendix 1: Peginterferon Drug Information

PEGINTERFERON DRUG INFORMATION

DESCRIPTION

A long-acting, synthetic interferon that enhances the antiviral immune response. Although peginterferon is approved for use as monotherapy or in combination with other antiviral medications for the treatment of chronic hepatitis C, ***current guidance recommends its use only in sofosbuvir- or simeprevir-based regimens and recommends against its use as monotherapy or as dual therapy in combination with ribavirin alone.***

FORMULATIONS

Two formulations are available for subcutaneous injection:

- Peginterferon alfa-2a (Pegasys®)
- Peginterferon alfa-2b (Peg-Intron®)

Although the two formulations are dosed differently, there is no demonstrated difference in efficacy. Note that dosing for Peg-Intron is more complicated than for Pegasys. (See *STANDARD DOSING* below.)

STANDARD DOSING

Peginterferon alfa-2a (Pegasys)

Pegasys is dosed 180 micrograms subcutaneously once weekly—regardless of weight.

Peginterferon alfa 2b (Peg-Intron)

Peg-Intron is administered subcutaneously, once weekly. The dosing chart below is based on a recommended dose of 1.5 micrograms (mcg) per kilogram per week (regardless of HCV genotype). Peg-Intron comes in four different vial strengths. Utilize the appropriate vial strength related to the patient's weight.

Body Weight (pounds)	Peginterferon alfa 2b Dosing (subcutaneously, once weekly)		
	Vial Strength (microgram/0.5 mL)	Dose to Administer (1.5 mcg/kg/wk)	Volume to Administer (mL)
<88	50	50	0.5
88–111	80	64	0.4
112–133	80	80	0.5
134–144	120	96	0.4
145–166	120	96	0.4
167–177	120	120	0.5
178–187	120	120	0.5
188–231	150	150	0.5
> 231	150	150	0.5